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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/052,803	11/07/2001	Fernand Labric	P/1259-637	3989

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EXAMINER	
JIANG, SHAOJIA A	

ART UNIT	PAPER NUMBER
1617	

DATE MAILED: 10/28/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/052,803	LABRIE, FERNAND	
	Examiner	Art Unit	
	Shaojia A. Jiang	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 August 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,13-19,22-24,35-41 and 44* is/are pending in the application.

4a) Of the above claim(s) *24 and 44* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-2, 13-19, 22-23, and 35-41* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *9/6/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This Office Action is in response to Applicant's amendment and response filed on August 11, 2005 wherein claims 1, 22, and 35 have been amended. Claims 3-12, 20-21, 25-34 and 42-43 are cancelled previously.

Currently, claims 1-2, 13-19, 22-24, 35-41 and 44 are pending in this application.

It is noted that claim 24 is withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected species, of record in the previous Office Action dated April 30, 2004. Note that new claim 44 is also directed to a non-elected species, same as claim 24. Thus, claim 44 is withdrawn from further consideration by the examiner, 37 CFR 1.142(b).

Note that Applicant's election without traverse of the species of EM-652.HCl in claim 17 for the SERM compound, 17β-estradiol in claim 20 for as an estrogen, and dehydroepiandrosterone (DHEA) for additional agent in claim 2, submitted April 30, 2002 has been recorded in the previous Office Action May 21, 2002.

Claims 1-2, 13-19, 22-23, and 35-41 are currently under examination on the merits.

The terminal disclaimer filed on August 11, 2005, disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of U.S. 6,710,059 has been reviewed and is accepted. The terminal disclaimer has been recorded.

The terminal disclaimer filed on August 11, 2005, with respect to the rejection of claims 1 and 22 made under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 10 of U.S. Patent No. 6,710,059 of record in the previous Office Action February 8, 2005, has been considered and found persuasive. Therefore, this obviousness-type double patenting rejection is withdrawn.

Applicant's amendment filed August 11, 2005 with respect to the objection to claim 35 for under 37 CFR 1.75(c), as being of an improper dependent claim, of record in the Office Action dated February 8, 2005 has been fully considered and is found persuasive since claim 35 has been amended. Therefore, this said objection is withdrawn.

Applicant's amendment and the book "A Textbook of Drug Design and Development" regarding "a prodrug" filed on August 11, 2005 with respect to the rejection of claims 1 and 22 made under 35 U.S.C. 112 second paragraph for the use of the indefinite recitation, i.e., the abbreviation, "DES", "a prodrug" of record stated in the Office Action dated February 8, 2005 have been fully considered and found persuasive only as to "DES" but are not deemed persuasive as to "derivative" and "derivatives" as further discussed below.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-2 and 22-23 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, for reasons of record stated in the Office Action dated February 8, 2005.

The recitations, "derivative" and “derivatives”, in the claims render claims 1-2 and 22-23 indefinite. The recitations, "derivative" and “derivatives” are not clearly defined in the specification. Hence, one of ordinary skill in the art could not interpret the metes and bounds as to these recitations in the claims, since one of ordinary skill in the art would clearly recognize that many widely varying groups could possibly substituting the compounds herein would read on the “derivative or derivatives " of the compounds.

Given the fact that any significant structural variation to a compound would be reasonably expected to alter its properties, e.g., physical, chemical, physiological effects and functions. Thus, it is unclear and indefinite as to the "derivative" of compounds herein encompassed thereby.

Therefore, the scope of claim is indefinite as to the composition encompassed thereby.

Note in the remarks filed August 11, 2005 that Applicant does not argue the rejection on "derivative" and “derivatives”.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1 and 13-16 are rejected under 35 U.S.C. 102(b) as being anticipated by Simard et al. (International Journal of Cancer (1997), 73(1), 104-112, "83" in PTO-1449 submitted November 7, 2001) for reasons of record stated in the Office Action dated February 8, 2005.

Simard et al. discloses a composition comprising 17β-estradiol (E2), the instant estrogen, and a simultanoues incubation with EM-652 or EM-800, the instant SERM compound, and a pharmaceutical diluent or carrier such as water in vitro. See abstract, page 104-105; Fig 2-12 at page 106-111. Thus, the testing results show that EM-652 or EM-800 as non-steroidal antiestrogens are useful in treating breast cancer in patients (see abstract), particularly including those woman patients who need to take estrogens daily for hormone replacement therapy (HRT).

Thus, the disclosure of Simard et al. anticipates claims 1 and 13-16.

Claims 1-2 and 13-16 are rejected under 35 U.S.C. 102(b) as being anticipated by Couillard et al. ("8" in PTO-1449 submitted November 1, 2004) for reasons of record stated in the Office Action dated February 8, 2005.

Couillard et al. discloses that administering estrone, the instant estrogen, to mice while co-administering EM-800 and DHEA in a composition with a pharmaceutical

diluent or carrier, is useful in inhibiting breast tumors or cancer growth in mice. See the entire article.

Thus, the disclosure of Couillard et al. anticipates claims 1-2 and 13-16.

Response to Argument

Applicant's arguments filed August 11, 2005 with respect to the two rejections made under 35 U.S.C. 102(b) as being anticipated by Simard et al. and Couillard et al. in the previous Office have been fully considered but they are not deemed persuasive to render the claimed invention patentable over the prior art as further discussed below.

Applicant argues that "both Simard and Couillard teach against estrogen. Couillard notes at abstract lines 6-7, "Estrone caused a 10-fold increase in ZR-75-1 tumor area . . ." ZR-75-1 is defined as human mammary tumor. Likewise, Simard states that estrogens play a predominant role in the development and growth of human breast cancer . . ." (Abstract, lines 1-2).

Applicant's argument is not found persuasive. Since first, the instant claims are directed to a pharmaceutical composition, which is a product claim not method claim. Thus, so long as Simard et al. discloses a composition comprising 17β-estradiol (E2), the instant estrogen, and a simultanoues incubation with EM-652 or EM-800, the instant SERM compound, and a pharmaceutical diluent or carrier such as water in vitro, or Couillard et al. discloses that administering estrone, the instant estrogen, to mice while co-administering EM-800 and DHEA in a composition with a pharmaceutical diluent or carrier, the prior art anticipates the claimed composition.

Second, as set forth in MPEP 2131.05, "Argument that the alleged anticipatory prior art is 'nonanalogous art' or 'teaches away from the invention' or is not recognized as solving the problem solved by the claimed invention, [are] not 'germane' to a rejection under section 102" (see also *Twin Disc. Inc. V. United States*, 231 USPQ 417, 424 (Cl.Ct. 1986). The question whether a reference "teach away" from the invention is inapplicable to an anticipation analysis (see also *Celeritas Technologies Ltd v. Rockwell International Corp.*, 150 F.3d 1354, 1361, 47 USPQ2d 1516, 1522-23 (Fde. Cir. 1999). Thus, in this case, Applicant's argument that "both Simard and Couillard teach against estrogen" is not germane to the 102 rejections herein.

For the above stated reasons, said claims are properly rejected under 35 U.S.C. 102(b). Therefore, said rejection is adhered to.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 17-19, 22-23, and 35-41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Simard et al. or Couillard et al. for reasons of record stated in the Office Action dated February 8, 2005.

The same disclosure of Simard et al. or Couillard et al. has been discussed in the 102(b) rejection set forth above.

The prior art does not expressly disclose the employment of a kit to store the compositions of Simard et al. or Couillard et al. The prior art does not expressly disclose the employment of the known pharmaceutically acceptable salt of the acid in a pharmaceutical composition or a kit.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to employ a kit for comprising the composition of Simard et al. or Couillard et al. and to employ the known pharmaceutically acceptable salt of the acid in a pharmaceutical composition or a kit, since the patient pack or kit and the pharmaceutically acceptable salts are all deemed obvious; they are all within the knowledge and conventional skills of pharmacologist to conveniently assist the user and prescriber for easy dispensary of the medication.

Claims 1-2, 13-19, 22-23, and 35-41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Luo et al. ("54", PTO-1449 submitted November 7, 2001) and Barrett-Connor et al. ("4", PTO-1449 submitted November 7, 2001), and Do Nascimento (of record) in view of Labrie et al. (WO 96/26201, PTO-1449 submitted November 7, 2001), for the same reasons of record in the Office Action dated February 8, 2005.

Luo et al. discloses that an estrogen, DHEA alone, or the particular SERM (antiestrogen), EM-800 alone (having 2S configuration and moieties convertible in vivo to hydroxyl), is known to be useful in a method of treating hyperlipidemia by decreasing serum lipid levels such as triglyceride and cholesterol levels. See abstract and page 4436 Fig. 1 "Structure of EM-800", page 4438 the left column "Effect on serum lipid

levels". Luo et al. further discloses that the combination of DHEA and EM-800 exerts more potent effect on reducing serum lipid levels than each compound used alone (page 4438 the left column "Effect on serum lipid levels" and page 4439 Fig. 4, and page 4443 the left column.

Barrett-Connor et al. teaches that SERMs are capable of lowering serum lipid levels to reduce the risk of coronary heart disease, as estrogen does. See abstract.

Do Nascimento teaches that the particular estrogen, 17β-estradiol, is useful in treating hypercholesterolemic patients (see abstract).

The prior art does not expressly disclose the employment of the combination of an estrogen such as 17β-estradiol and the particular SERM, EM-652.HCl, or further combining with DHEA in a pharmaceutical composition.

Labrie et al. (WO 96/26201) discloses that both EM-800 and EM-652 or EM-652.HCl are antiestrogens (SERMs), and EM-800 has moieties convertible in vivo to hydroxyl to become EM-652. Thus, EM-800 is a metabolite of EM-652, having the same functional property and activity.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to employ of the combination of an estrogen such as 17β-estradiol and the particular SERM, EM-652.HCl, or to further combine with DHEA, in a pharmaceutical composition.

One having ordinary skill in the art at the time the invention was made would have been motivated to employ the combination of an estrogen such as 17β-estradiol and the particular SERM, EM-652.HCl, or to further combine with DHEA, in a

pharmaceutical composition, since estrogens such as 17β-estradiol and DHEA are well known in the art to be used in methods of treating hyperlipidemia by decreasing serum lipid levels such as triglyceride and cholesterol levels according to the cited prior art herein. Moreover, the particular SERM, EM-800, a known metabolite of EM-652 (convertible in vivo to hydroxyl to become EM-652), alone or in combination with an estrogen such as DHEA, is known to be useful in a method of treating hyperlipidemia by decreasing serum lipid levels such as triglyceride and cholesterol levels according to Luo et al.

Therefore, one of ordinary skill in the art would have reasonably expected that combining an estrogen such as 17β-estradiol and the particular SERM, EM-652.HCl, or further combining with DHEA, all known useful for the same purpose, i.e., treating hypercholesterolemia, would improve the therapeutic effects for treating the same disorder, hypercholesterolemia, and/or would produce additive therapeutic effects in treating the same. See *In re Kerkhoven*, 205 USPQ 1069 (CCPA 1980) regarding combination inventions. It is considered prima facie obvious to combine two active composition components into a single composition to form a third composition useful for the very same purpose.

Further, the teachings of Luo et al. that the combination of DHEA and EM-800 exerts more potent effect on reducing serum lipid levels than each compound used alone clearly provides the motivation of the instant claimed method employing the combination of EM-652, 17β-estradiol and DHEA.

Furthermore, one of ordinary skill in the art would have been motivated to prepare a kit comprising the same composition because the preparation of a kin comprising a pharmaceutical composition is considered well in the competence level of an ordinary skilled artisan in pharmaceutical science, involving merely routine skill in the art.

Thus the claimed invention as a whole is clearly prima facie obvious over the teachings of the prior art.

Applicant's remarks filed August 11, 2005 with respect to the rejection made under 35 U.S.C. 103(a) as being unpatentable over Luo et al. and Barrett-Connor et al. and Do Nascimento (of record) in view of Labrie et al. of record in the previous Office Action February 8, 2005 have been fully considered but are not deemed persuasive as to the nonobviousness of the claimed invention over the prior art as further discussed below.

The examiner notes that DHEA is not covered by estrogen as Applicant asserts in the remarks. However, claim 2 clearly recites DHEA, and claim 1 does not exclude additional, unrecited elements such as DHEA since the transitional phrase "comprising" is employed in the instant claimed composition. Applicant is requested to note that the transitional term "comprising" is inclusive or open-ended and does not exclude additional, unrecited elements or method steps. See MPEP 2111.03.

Thus, this rejection is maintained.

In view of the rejections to the pending claims set forth above, no claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Jiang, whose telephone number is (571)272-0627. The examiner can normally be reached on Monday-Friday from 9:00 to 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan, Ph.D., can be reached on (571)272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

S. Anna Jiang, Ph.D.
Primary Examiner
Art Unit 1617
October 19, 2005